Chen, Y. "Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood" Chest 95: 1004-1007, 1989.

ABSTRACT. The synergism of passive smoking and artificial feeding on hospitalization for respiratory illness in early childhood was examined among 2,227 subjects born in the last quarter of 1983 in Chang-Ning District, Shanghai, People's Republic of China. The eligible families were visited by the trained interviewers. A loglinear model shows no interaction on a multiplicative scale between these two factors on the frequency of hospitalization for respiratory illness during the first 18 months of life. However, the synergism of passive smoking and artificial feeding on the consequence was detected by using Rothman's approach that these two synergistic agents worked together producing a detrimental effect much more than that expected by their separate actions. These data suggested that it is more important to stop smoking in the families where the infants were artificially fed.

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Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood*

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The synergism of passive smoking and artificial feeding on hospitalization for respiratory illness in early childhood was examined among 2,227 subjects born in the last quarter of 1963 in Chang-Ning District, Shanghai, People's Republic of China. The eligible families were visited by the trained interviewers. A loglinear model shows no interaction on a multiplicative scale between these two factors on the frequency of hospitalization for respiratory illness during the first 18 months of life. However, the synergism of passive smoking and artificial feeding on the consequence was detected by using Rothman's approach that these two synergistic agents worked together producing a detrimental effect much more than that expected by their separate actions. These data suggested that it is more important to stop smoking in the families where the infants were artificially fed. *(Chest 1989; 95:1004-07)*

ICD = International Classification of Disease; ID = incidence density; IDR = incidence density ratio

Our earlier papers presented that household exposure to tobacco smoke and artificial feeding are both important risk factors of hospitalization for respiratory illness during a child's first 18 months of life.[1,2] The combined effect of these two factors seems even greater than that expected by their separate actions.[2] Although this picture is not statistically significant in the above study due to limited sample size, it was hypothesized that there may be synergism between these two agents that the infants artificially fed are more vulnerable to be hospitalized for respiratory illness caused by passive smoking in early childhood. In this analysis, the data of Chang-Ning Epidemiologic Study of Children's Health[3] was further examined to identify the potential synergism of passive smoking and artificial feeding on hospitalization for respiratory illness during the first 18 months of life.

METHODS

The study covers the total area of Chang-Ning District, Shanghai, People's Republic of China. All 2,315 live birth babies born in the last quarter of 1963 in this area were selected as the study population. The survey was conducted during the period from March to June 1965 when the children just reached the age of one and half years. Each questionnaire was administered and recruited to each child's home by trained interviewers. This questionnaire asked about dates and causes of hospitalization from birth to 18 months, smoking habits of parents and other household individuals and type of feeding of the child. The questionnaire also included questions on sociodemographic data, baby's characteristics, residential conditions and household environmental exposure, parental education, and all family members' chronic respiratory diseases during the child's first 18 months of life. Among the eligible sample, 2,227 questionnaires were completed, with response rate of 96 percent. Selected characteristics of the population are shown in Table 1.

The diagnosis of hospitalization for respiratory illness include ICD (9th revision)* codes 460, 462-466, 480, 485-487, 492, 493, 786.2.

The children studied were divided into three passive smoking

Table 1—*Frequency of Selected Characteristics of the Population*

	No.	%	Mean	SD
Sex				
Boys	1155	51.9		
Girls	1072	48.1		
Multiple birth				
No	2184	98.1		
Yes	43	1.9		
Feeding type				
Breast or mixed	1463	66.6		
Artificial	744	33.4		
Day-care nursery				
No	1720	77.2		
Yes	507	22.8		
Father's education				
University	200	9.5		
Secondary	1999	89.5		
Primary	28	1.3		
Coal used for cooking				
No	980	44.0		
Yes	1247	56.0		
Adult(s) in family with chronic respiratory disease				
Yes	396	17.8		
No	1831	82.2		
Cigarettes smoked daily by family member(s)				
None	481	21.6		
1-19	993	44.6		
20+	753	33.8		
Birth weight, kg			3.2	0.44
Maternal age at birth, yr			28.2	3.01
Average income, yuan			36.8	9.51
Number of rooms			2.5	1.20
Total living area, m²			25.0	19.46
Average living area per person, m²			5.4	4.32

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groups according to total number of cigarettes smoked daily by family members: none, 1 to 19 cigarettes/day, and 20+ cigarettes/day; and two feeding groups: a completely artificially fed group which consisted of the infants who had never been breast-fed and a group of breast-fed infants which consisted of those who were fully or partially breast-fed at any time in the first ten months of life.

Incidence density (ID) was used to measure the frequency of hospitalization.[3] The point and interval estimation for Rothman's index S was used to measure the synergistic effect of passive smoking with artificial feeding upon hospitalization on an additive scale.[4] Confounding factors were adjusted by stratified analysis. Denoting the standardized incidence density for risk indicator category i, j as SIDij, the Rothman's index of the joint risk-indicator-specific sets of strata is computed by

$$Sij = \frac{SIDij - SIDoo}{SIDio + SIDoj - 2SIDoo},$$

and taking for the pooled point estimate

$$S = \frac{Wij^{*}Sij}{Wij^{*}},$$

$$Wij^{*} = WijEij.$$

Here, Eij is the corresponding theoretical joint effect under independence, and Wij is the weight for that category. The standard error of the natural logarithm of S was evaluated by using first order Taylor series approximation.[4]

Results

There were 1,746 smoking families, 78.4 percent of the total, in which (786) only the father smoked, in 261 only another family members smoked, and in 699 both father and other family members smoked. No mothers who were smokers were found. The crude IDRs were 2.5 for 20+ cigarettes per day group and 1.7 for 1 to 19 cigarettes per day compared to nonsmoking families. The influence of passive smoking on the other diagnostic categories is not statistically significant. The independent effects of passive smoking have been detailed elsewhere.[3]

In this study, artificial feeding is another important risk factor of hospitalization for respiratory illness in early childhood. One third of the children were totally artificially fed up to ten months. The frequency of hospitalization for respiratory illness among artificially fed children is about two times higher than that among breast-fed ones (IDR = 1.9, $p<0.01$). Table 2 presents the incidence density of hospitalization for respiratory illness during the first 18 months of life by smoking status of family members and children's feeding type. It shows that the risk increased with the increasing of smoking amount by family members among these artifically fed children more rapidly than that among the breast-fed ones. It seems that the artificially fed children are more susceptible to respiratory illness due to household exposure to cigarette smoke. Figure 1 pictures a framework of the combined effect of passive smoking with artificial feeding on the inpatient admission for respiratory illness during the first 18 months of life.

Table 3 shows the IDRs of hospitalization for respiratory illness of various groups combined passive smoking with feeding type compared with the breast-fed children without exposure to cigarette smoke in the household before and after adjusting covariates including sex, birth weight, and father's educational status. Rothman's approach detected a significant synergistic effect of these two factors on the hospitalization for respiratory illness during the first 18 months of life. The pooled point estimate of Rothman's index $\hat{S}$ is 3.8 with the 90 percent confidence interval from 1.24 to 11.34 after adjusting the confounding factors. Analysis by using loglinear model shows the interaction on a multiplicative scale between these two factors is not statistically significant.

Table 2—*Incidence Densities of Hospitalization for Respiratory Illness in Early Childhood by Passive Smoking and Feeding Type*

	Cigarettes Smoked Daily by Family Members			
Feeding Type	None	1-19	20+	Total
Breast or mixed				
Cases	13	34	35	82
Person-years	445.5	1011.0	768.0	2224.5
ID (/year)	0.0292	0.0336	0.0456	0.0369
Artificial				
Cases	9	36	35	80
Person-years	276.0	478.5	361.5	1116.0
ID (/year)	0.0326	0.0752	0.0968	0.0717
Total				
Cases	22	70	70	162
Person-years	721.5	1489.5	1129.5	3340.5
ID (/year)	0.0304	0.0470	0.0620	0.0485

Discussion

This report depicts the joint effect of passive smoking and artificial feeding on the hospitalization for respiratory illness during the first 18 months of life that passive smoking worked together with artificial feeding would produce a detrimental effect much

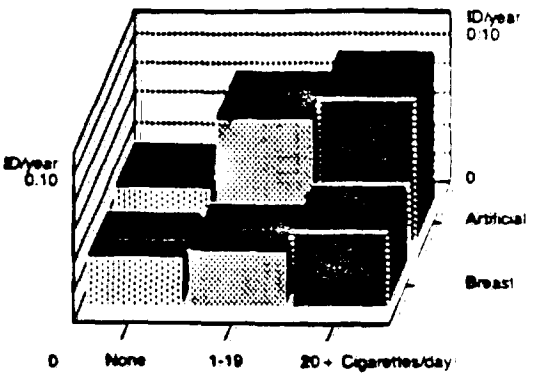

Figure 1. Combined effect of passive smoking and artificial feeding on hospitalization during first 18 months of life.

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Table 3—*Synergism of Passive Smoking and Feeding Type on Hospitalization for Respiratory Illness in Early Childhood*

Cigarettes smoked daily by family member(s)	Feeding type	Unadjusted IDR	Unadjusted $ij	Adjusted* IDR	Adjusted* $ij
None	Breast or mixed †	1.00		1.00	
	Artificial	1.12		1.10	
1-19	Breast or mixed	1.15		1.22	
	Artificial	2.58	5.90	2.91	5.97
20†	Breast or mixed	1.56		1.64	
	Artificial	3.32	3.41	3.37	3.20

*Adjusted variables included: sex, birth weight and father's education.

†Reference group.

more than that expected by the separate action of these two factors.

The reports concerning respiratory infection and artificial feeding have been conflicting. Several studies have shown a significant association between them,[7-15] but not others.[16-20] Although information needed to evaluate the conclusions was not included in most of studies. Methodologic problems might explain a part of these differences.[21,22] The results of this report based on a larger study population add weight to our earlier conclusion that artificial feeding increased a risk of hospitalization for respiratory illness in early childhood.

Although many studies pictured an increased risk of respiratory infection associated with passive smoking and artificial feeding, none explicitly described the interaction between them with the health outcome. The possibility of interaction was mentioned only in the study by Watkins et al[8] besides our earlier report.[9] After examining the type of feeding and respiratory infection in the first year of life, in the study by Watkins et al,[8] they found that high-risk infants appeared to benefit more from breast-feeding. The estimated incidence of respiratory infection in artificially fed infants, predicted by fitting a general interactive model to the data, ranged from 42 percent in boys with more than two siblings, whose parents smoked and mothers reported cough and phlegm to 4.9 percent in girls with no siblings neither of whose parents smoked nor reported cough or phlegm. In the breast-fed infants, the comparable estimates were 30 percent to 2.9 percent. The difference between 12 percent predicted attributable risk reduction for high-risk infants and 2 percent for low-risk infants reflects the interaction between type of feeding and mixed effect of sex, siblings, parental smoking status, and maternal respiratory troubles. But the interactive effect of parental smoking with type of feeding was not isolated in this study.

In this study, the child's sex is another predictor of hospitalization for respiratory illness. The ID was 0.063/year in boys vs 0.042/year in girls. The synergistic effect of passive smoking and artificial feeding is evident in both groups. The incidence density ratios were 3.2 in artificially fed boys whose family members smoked, compared with breast-fed boys, and 1.2 in those only whose family members smoked and 1.1 in those only artificially fed, and they were 3.2, 1.5 and 1.1, respectively, in girls.

For epidemiologic studies of the health effects of infant feeding, various potential sources of bias are considerable. In this study, all infants were classified dichotomously. The breast-feeding group consisted of infants who were completely breast-fed during the first ten months of life, some who received only a few feedings of human milk, and others who fit between these two extremes. The effect of artificial feeding on the hospitalization for respiratory illness is probably underestimated.[2,23] Although the duration of breast-feeding can be alternatively used to evaluate the protective effect of human milk feeding, selection bias will probably emerge.[23] Since infant feeding is a one-way street, the children are often placed on artificial feeding when they fail to thrive and become ill, and children who are breast-fed exclusively for a prolonged period of time are likely to be extremely healthy.[23-25] As Kramer said, the investigator must often navigate between the Scylla and Charybdis.[23] Dichotomous classification of infant feeding in this report, for another reason, can keep the number of each subgroup sufficient for stratified analysis.

In most studies from developed countries, it seems a knotty problem to distinguish between the effect of maternal smoking during pregnancy and the effect of environmental exposure to cigarette smoking.[26] However, young women smoking is very rare here, and no young mother who smoked was detected in this study and in others as well.[1,26,27] Other potential sources of bias have been discussed in detail elsewhere.[3]

Many studies have explored the possible mechanisms of the protective effect of breast feeding and the detrimental effect of passive smoking on the health outcomes.[28-30] Breast milk is considered the best infant food due to its cleanliness, nutrition and content of a number of antiinfectious agents which make infants able to resist the invasion of certain pathogenic agents. Environmental tobacco smoke can be a substantial contributor to the level of indoor air pollution concentrations of the respiratory particles benzene, acrolein, N-nitrosamine, pyrene, and carbon monoxide.[30] Although the evidence is not yet convincing for the synergism of passive smoking and type of feeding, this will not stop us from tendering advice that it is more important to keep the artificially fed children from tobacco smoke pollutants.

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